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A Versatile Synthesis of Various Substituted Taurines from Vicinal Amino Alcohols and Aziridines

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Taurine and structurally diverse substituted taurines have been synthesized by peroxyformic acid oxidation of the thiazolidine-2-thione intermediates generated from vicinal amino alcohols or aziridines and carbon disulfide. The stereochemistry and mechanisms of the reactions are discussed. The method is a salt-free and versatile route, convenient in terms of purification, and can be used to synthesize optically active substituted taurines.

Introduction

Taurine and substituted taurines are 2-aminoalkanesulfonic acids, a class of important aminoalkanesulfonic acids,[1] with taurine the simplest and most well-known of these compounds. It was discovered more than 200 years ago and exhibits many important biological activities.[2] D-Cysteinolic acid [(*S*)-2-amino-3-hydroxy-1-propanesulfonic acid] was first isolated from the red alga *Polysiphonia fastigiata* in 1957.[3] Both are naturally occurring amino sulfonic acids and are involved in various physiological processes.[2,4,5] Taurine and some substituted taurines play important roles in biological and medicinal chemistry.[1,2,4,6] They have been widely used as sulfur analogues of amino carboxylic acids in the preparation of sulfonopeptides, peptidomimetics with a tetrahedral structural feature that act as enzyme inhibitors, in the search for peptidomimetic drugs.[1,7]

Several syntheses of taurine and substituted taurines have been developed.[1] They include the sulfite displacement of vicinal aminoalkyl halides,[8] amino-hydroxy-methanesulfonates[9] or hydrogen sulfates,[10] the addition of sodium bisulfite to nitroolefins followed by reduction,[11] the peroxyformic acid oxidation of vicinal aminoalkyl thioacetates,[7b,12] and the aminosulfonation of olefins and subsequent hydrolysis.[13] Recently, our group has focused on the development of convenient and efficient routes to the synthesis of diverse substituted taurines and reported two new synthetic methods that employ three-membered heterocycles as starting materials. We synthesized substituted taurines by the ring-opening reaction of aziridines with sodium bisulfite[14] or thioacetic acid followed by peroxyformic acid oxidation and hydrolysis.[15] We also performed a ring-opening of episulfides with amine/ammonia followed by peroxyformic acid oxidation to produce these compounds.[16] Enders and co-workers reported an efficient asymmetric synthesis of 2-substituted and 1,2-disubstituted taurine derivatives through aza-Michael addition of enantiopure hydrazines to α,β-unsaturated sulfonates in the presence of Lewis acid catalysts.[17] They also further converted substituted taurine derivatives into substituted β-sultams and γ-sultones.[17b,18] Recently, they reported a new asymmetric synthesis of *anti*-1,2-disubstituted taurine derivatives by the nucleophilic addition of phenylmethanesulfonate to various *N*-acylimines in the presence of 1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose as a chiral auxiliary.[19]

It has been reported that taurine can be synthesized from heterocyclic thiazoline by bromine oxidation.[20] However, the thiazolines need to be prepared from vicinal amino mercaptans, most of which are commercially unavailable and are uncomfortably odorous. On the other hand, amino mercaptans can be oxidized to taurines directly. As the analogues of thiazolines, we assumed that heterocyclic thiazolidine-2-thiones could be oxidized to taurines with peroxyformic acid. They have been synthesized conveniently from vicinal amino alcohols and carbon disulfide.[21] Many vicinal amino alcohols are commercially available, but they can also be prepared by the reduction of amino acids. Herein, we present an efficient, and versatile method for the synthesis of taurines from vicinal amino alcohols via five-membered heterocyclic thiazolidine-2-thiones as the key intermediates.

Results and Discussion

First, a series of structurally diverse thiazolidine-2-thiones **2** were synthesized from the corresponding vicinal

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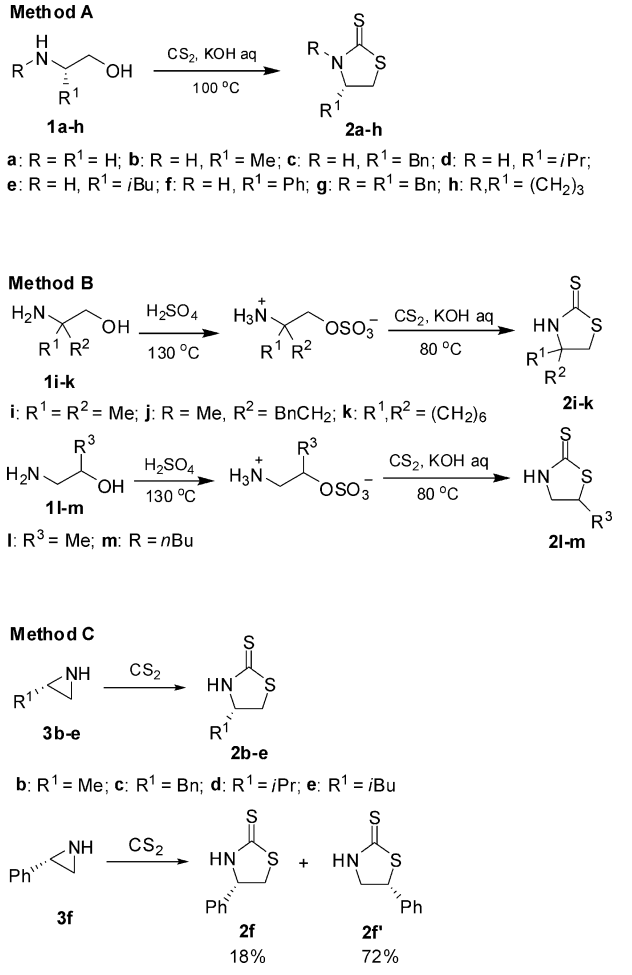
amino alcohols **1** by a modified literature method.[22] 4-Substituted thiazolidine-2-thiones **2a**–**h** were prepared in high yields (68–95%) by the direct reaction of amino primary alcohols **1a**–**h** and carbon disulfide in the presence of potassium hydroxide (Scheme 1, Method A; Table 1, entries 1–8). However, 4,4-disubstituted thiazolidine-2-thiones **2i**–**k** and 5-substituted thiazolidine-2-thiones **2l**,**m** were obtained in relatively low yields (18–49%) by the direct method because of steric hindrance. Oxazolidine-2-thiones and thiazolidine-2-thiones were both obtained in ratios of 80:18 to 51:49. Le Corre and co-workers[22] have also reported that oxazolidine-2-thiones are the major products in most cases. Thus, we needed to search for an efficient synthesis of 4,4-disubstituted and 5-substituted thiazolidine-2-thiones. Fujita et al.[23] conducted the reaction of 1-amino-2-propyl hydrogen sulfate with CS_2, which afforded 5-methylthiazolidine-2-thione (**2l**) in 48% yield. Thus, activation of the hydroxy group could improve the yields in the synthesis of 5-substituted thiazolidine-2-thiones. After activating the hydroxy group of amino secondary alcohols **1l**,**m** with chlorosulfonic acid[23] or sulfuric acid[10,14] and prolonging the reaction time, 5-substituted thiazolidine-2-thiones **2l**,**m** were synthesized in high yields (87–90%) via amino alcohol hydrogen sulfates as intermediates (Scheme 1, Method B; Table 1, entries 12 and 13). 4,4-Disubstituted thiazolidine-2-thiones **2i**–**k** were also prepared in improved yields (43–53%) by activating the hydroxy group (Scheme 1, Method B; Table 1, entries 9–11). Optically active amino primary alcohols **1b**–**h** gave rise to enantiomerically pure thiazolidin-2-thiones **2b**–**h** with the same configuration as the substrates[22] (Table 1, entries 2–8). However, with secondary alcohols, 5-substituted thiazoldine-2-thiones with the reverse configuration were obtained. For example, starting from *trans*-2-aminocycloalkanols **1n**,**o**, *cis*-4,5-disubstituted bicyclic thiazolidine-2-thiones, namely, *cis*-7,9-thiazabicyclo[4.3.0]nonane-8-thione (**2n**) and *cis*-2,4-thiazabicyclo[3.3.0]octane-3-thione (**2o**), were obtained.

The reaction of aziridines and carbon disulfide is an alternative route to the synthesis of thiazolidine-2-thiones (Scheme 1, Method C).[24] Optically active (*S*)-2-alkylaziridines **3b**–**e** reacted with carbon disulfide to generate (*S*)-4-alkylthiazolidine-2-thiones **2b**–**e**. However, aromatically substituted (*S*)-2-phenylaziridine (**3f**) gave rise to a mixture of (*S*)-4-phenylthiazolidine-2-thione (**2f**) and (*R*)-5-phenylthiazolidine-2-thione (**2f′**) in a ratio of 1:4 under the same conditions. Their configurations and optical purities were determined by comparison with reported specific rotations[25] and revealed that 2-arylaziridines were preferentially attacked at the benzylic carbon atom by the carbon disulfide due to the stability of the *p*-π conjugation in the transition state of the nucleophilic ring-opening step, which occurs by an S_N2 process. The detailed reaction processes are shown in Scheme 2. Aziridinocycloalkanes **3n**,**o** were prepared from *trans*-2-aminocycloalkanols **1n**,**o**.[14,26] 7-Azabicyclo[4.1.0]heptane (**3n**) produced *trans*-7,9-thiazabicyclo[4.3.0]nonane-8-thione (**2p**), but 6-azabicyclo[3.1.0]hexane (**3o**) failed to react due to the strain hindrance effects (Scheme 3), as reported previously.[27]



Scheme 1. Synthesis of thiazolidine-2-thiones.

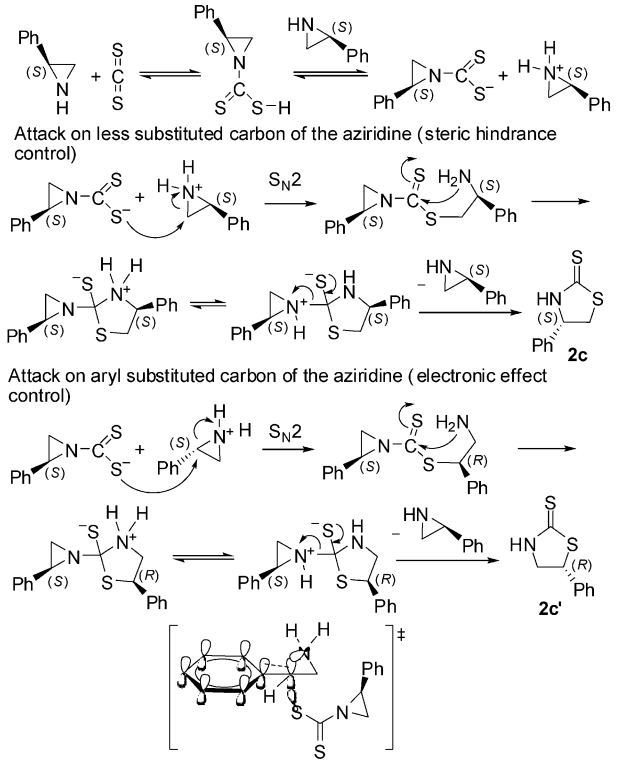
The synthesized thiazolidine-2-thiones **2** were oxidized with peroxyformic acid, which was prepared by mixing formic acid (88%) and hydrogen peroxide solution (30%). Most of the thiazolidine-2-thiones were oxidized to taurines **4** in good-to-excellent yields. However, in some cases, especially in the oxidation of 5-substituted thiazolidine-2-thiones, repetitive oxidation was necessary. After several attempts, we found that a high concentration of peroxyformic acid, generated from hydrogen peroxide (30%) and anhydrous formic acid (98%) (1:5, v/v), gave the best result in the oxidation reaction (Scheme 4).[28]

Various substituted thiazolidine-2-thiones **2** were oxidized to the corresponding substituted taurines **4**, including taurine, 1- and 2-substituted taurines, 2,2-disubstituted taurines, *N*-substituted taurines, and cyclic taurines (shown in Table 1). Taurine **4q**, the enantiomer of D-cysteinolic acid, was synthesized from L-cysteine methyl ester hydrochloride (Table 1, entry 17). Both *cis*- and *trans*-cyclic taurines were prepared from *trans*-2-aminocycloalkanols directly or via their aziridine derivatives as intermediates. Optically pure amino alcohols gave rise to enantiomerically pure taurines without loss of optical purity, as revealed by a comparison of their specific rotations with reported values. Chiral 2-alkylaziridines gave rise to optically pure taurines

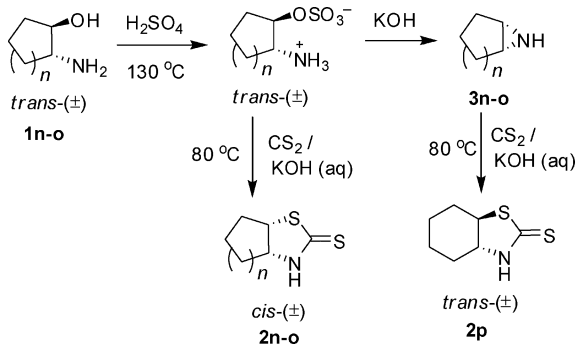
Table 1. Synthesis of structurally diverse taurines.

Entry	Amino alcohol / aziridine	Thiazolidine-2-thione	Yield (%)[a]	Taurine	Yield (%)
1	 **1a**	 **2a**	92	 **4a**	93
2	 **1b**  **3b**	 **2b**	94 58	 **4b**	94
3	 **1c**  **3c**	 **2c**	88 67	 **4c**	83
4	 **1d**  **3d**	 **2d**	85 90	 **4d**	100
5	 **1e**  **3e**	 **2e**	95 60	 **4e**	81
6	 **1f**  **3f**	 **2f** 18% +  **2f′** 72%	89 90	 **4f**  **4f′**	80 86 [d]
7	 **1g**	 **2g**	81	 **4g**	86
8	 **1h**	 **2h**	68	 **4h**	85
9	 **1i**	 **2i**	49 53[b]	 **4i**	92
10	 (±) **1j**	 (±) **2j**	35 43[b]	 (±) **4j**	90
11	 **1k**	 **2k**	19 45[b]	 **4k**	82
12	(±) **1l**	(±) **2l**	20 90[b]	(±) **4l**	96
13	(±) **1m**	(±) **2m**	18 87[b]	(±) **4m**	88
14	(±) **1n**	(±) **2n**	20 63[b]	(±) **4n**	90
15	(±) **1o**	(±) **2o**	75[b]	(±) **4o**	95
16	**3n**	(±) **2p**	68	(±) **4p**	92
17	**1q**	**2q**	67[c]	**4q**	93

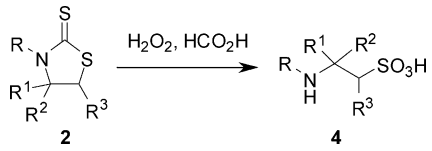
[a] Yields of isolated products prepared by Method A or C. [b] Yields of isolated products prepared by Method B. [c] Overall yield from the cyclization and reduction (see the Supporting Information). [d] Yield from separated **2f′**.



Scheme 2. Reactions of 2-arylaziridines with carbon disulfide.



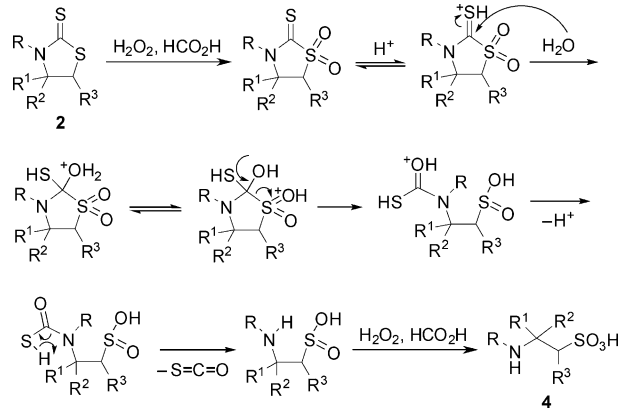
Scheme 3. Synthesis of *cis*- and *trans*-bicyclic thiazolidine-2-thiones from cyclic vicinal amino alcohols.



Scheme 4. Synthesis of taurines from thiazolidine-2-thiones.

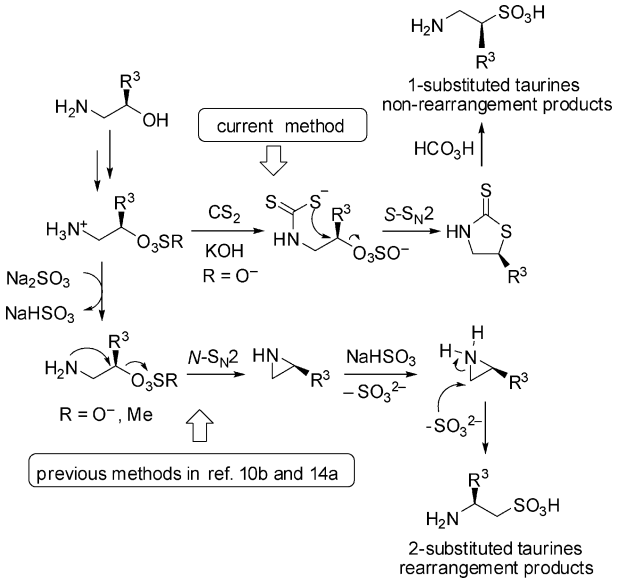
with the same configuration, whereas 2-arylaziridine produced enantiopure 1-aryltaurines mainly with the opposite configuration.

As for the oxidation mechanism, we initially assumed that thiazolidine-2-thiones first underwent hydrolysis to give amino mercaptans under acidic reaction conditions and that these were then oxidized to substituted taurines with performic acid. To verify the reaction mechanism thiazolidine-2-thiones **2c** and **2f** were dissolved in formic acid and the resulting solutions were stirred for 1 d. However, no hydrolysis was observed. Fujita et al. reported that thiazolidinethione **2l** was hydrolyzed in 6 mol/L HCl by heating at reflux for a week to yield the corresponding amino mercaptan.[23] Both our results and those previously reported[23] indicate that thiazolidine-2-thiones are hardly hydrolyzed directly under our reaction conditions. It has been reported that α-oxo sulfones are unstable because their carbonyl group is a stronger electrophile than those in ketones and esters due to the existence of the vicinal sulfone group and can undergo hydrolysis,[29] alcoholysis,[29] and aminolysis[30] to generate alkanesulfinic acids and ester and amide derivatives, respectively. Thus, we assumed that thiazolidine-2-thiones are oxidized to thiazolidine-2-thione 1,1-dioxides, cyclic sulfur analogues of α-oxo sulfones, which readily undergo acid-catalyzed hydrolysis to generate 2-aminoalkanesulfinic acids by the loss of a molecule of S=C=O under the reaction conditions. The 2-aminoalkanesulfinic acids are then oxidized to the taurines with performic acid (Scheme 5).



Scheme 5. Proposed mechanism for the oxidation of thiazolidine-2-thiones to substituted taurines with performic acid.

Substituted taurines have previously been prepared from vicinal amino alcohols by the displacement of methanesulfonate[9] or hydrogen sulfate.[10b,14a] However, amino secondary alcohols gave rise to 2-substituted taurines, like amino primary alcohols, by an intramolecular rearrangement;[14a] they cannot be used to synthesize 1-substituted taurines. Importantly, compared with the previous methods,[10b,14a] 1-substituted taurines can be prepared from amino secondary alcohols by the current route, avoiding the rearrangement step, because after neutralization, the free amino group first reacts with carbon disulfide to generate an *N*-acyl amino alcohol hydrogen sulfate that can only undergo an intramolecular sulfur S_N2 reaction (not the nitrogen S_N2 reaction because *N*-acylation decreases the nucleophilicity of the nitrogen atom; Scheme 6). In addition, the current method is a salt-free procedure and so does not require tedious desalting work to obtain water-soluble taurines. Thus, it is indeed a convenient procedure in terms of purification and practical for large-scale preparation.



Scheme 6. Comparison on application of vicinal amino secondary alcohols in synthesis of substituted taurines in the current and previous methods.

Conclusions

Taurine and a range of substituted taurines have been synthesized efficiently by the oxidation of thiazolidine-2-thiones, which were prepared conveniently from the corresponding amino alcohols or aziridines. Compared with the previous synthetic method, the new route described herein can be used for the synthesis of 1-substituted, 2-substituted, 2,2-disubstituted, and *N*-substituted taurines, including linear, cyclic, and optically active taurines. Furthermore, this method is an inexpensive, versatile, and salt-free procedure for the synthesis of highly pure diverse taurines in the laboratory as well as in large-scale industrial production.

Experimental Section

General: Melting points were determined with a melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded at 200, 300, or 400 MHz in $CDCl_3$, [D$_6$]DMSO, or D_2O with TMS or DOH as the internal standards. ^{13}C NMR spectra were recorded at 50.3, 75.5, or 100.6 MHz in $CDCl_3$, D_2O, or HCO_2H with $CDCl_3$ or HCO_2H as the internal standards (HCO_2H: δ = 166.3 ppm). IR spectra were determined directly. MS spectra were obtained with an ESI mass spectrometer. HRMS spectra were recorded with an LC/MSD TOF mass spectrometer. Optical rotations were measured with a polarimeter and a thermally jacketed 10 cm cell (concentration *c* expressed as g/100 mL). Melting points were measured with a Yanaco MP-500 melting point apparatus. NMR spectra were recorded with Varian Mercury 200 (200 MHz), Varian Mercury Plus 300 (300 MHz), or Bruker 400 AMX (400 MHz) spectrometers. Mass spectra were obtained with a Bruker ESQUIRE LCTM ESI ion trap mass spectrometer. HRMS data were obtained with an Agilent LC/MSD TOF mass spectrometer. IR spectra were determined with a Bruker Tensor 27 FT-IR spectrometer. Optical rotations were measured with a Perkin Elmer 741 polarimeter.

General Procedure for the Preparation of Thiazolidine-2-thiones (Method B): A solution of chlorosulfonic acid (1.4 g, 0.8 mL, 12 mmol) in anhydrous diethyl ether (5 mL) was added dropwise to a solution of amino alcohol (10 mmol) dissolved in anhydrous diethyl ether (15 mL) and cooled in an ice/water bath. The resulting mixture was stirred for 1 h. The precipitates were filtered and washed with ethanol twice and diethyl ether twice to afford solid amino alcohol hydrogen sulfate.[23]

Alternatively, a cold mixture of sulfuric acid (98%, 1 g) and water (1 mL) was added to the amino alcohol (10 mmol) in water (0.6–2.0 mL) at 0–5 °C. The mixture was heated to 120–130 °C for 0.5 h and then water was carefully distilled off in vacuo to afford solid amino alcohol hydrogen sulfate.[10b]

An aqueous solution of KOH (6.5 mL of 6.2 mol/L) was added to the prepared amino alcohol hydrogen sulfate and carbon disulfide (2.5 mL, 40 mmol) was then added. The resulting solution was heated at reflux at 80 °C in an oil bath for 3.5 h. After cooling to room temperature, the reaction mixture was extracted with dichloromethane (3 × 20 mL). The combined organic layers were dried with Na_2SO_4. Total removal of the solvent under reduced pressure gave the crude product, which was purified by recrystallization or by column chromatography on silica gel eluted with petroleum ether (60–90 °C)/ethyl acetate (2:1, v/v) to give the product as colorless crystals.

(±)-4-Methyl-4-phenethylthiazolidine-2-thione (2j): Colorless crystals; yield 1.02 g, 43%; m.p. 143–145 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.78 (br. s, 1 H, NH), 7.32–7.26 (m, 2 H, ArH), 7.22–7.17 (m, 3 H, ArH), 3.44 (d, *J* = 11.1 Hz, 1 H, CH_2S), 3.24 (d, *J* = 11.1 Hz, 1 H, CH_2S), 2.75–2.69 (m, 2 H, CH_2Ar), 2.09–2.02 (m, 2 H, CH_2), 1.52 (s, 3 H, Me) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 198.9, 140.4, 128.6, 128.2, 126.3, 70.3, 43.7, 41.7, 30.6, 25.3 ppm. IR ($CDCl_3$): $\tilde{\nu}$ = 3134 (NH), 3024 (ArH), 1492 (C=S) cm^{-1}. MS (ESI): *m*/*z* = 238.2 [M + H]$^+$, 260.1 [M + Na]$^+$. HRMS (ESI): calcd. for $C_{12}H_{16}NS_2$ [M + H]$^+$ 238.0718; found 238.0717.

3-Thia-1-azaspiro[4.6]undecane-2-thione (2k): Colorless crystals; yield 905 mg, 45%; m.p. 156–158 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.68 (br. s, 1 H, NH), 3.30 (s, 2 H, CH_2S), 2.01–1.89 (m, 4 H, 2 CH_2), 1.62–1.45 (m, 8 H, 4 CH_2) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 198.3, 74.3, 44.9, 38.8, 29.4, 22.9 ppm. IR ($CDCl_3$): $\tilde{\nu}$ = 3139 (NH), 1494 (C=S) cm^{-1}. MS (ESI): *m*/*z* = 202.1 [M + H]$^+$, 224.0 [M + Na]$^+$. HRMS (ESI): calcd. for $C_9H_{16}NS_2$ [M + H]$^+$ 202.0718; found 202.0715.

(*R*)-5-Phenylthiazolidine-2-thione (2f′): Colorless crystals; yield 1.40 g, 72%; m.p. 138–140 °C. $[\alpha]_D^{20}$ = +133.7 (*c* = 0.38, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.38 (br. s, 1 H, NH), 7.26–7.43 (m, 5 H, ArH), 5.18 (dd, *J* = 7.8, 8.1 Hz, 1 H, CHS), 4.29 (dd, *J* = 8.1, 11.3 Hz, 1 H, CH_2N), 4.01 (dd, *J* = 7.5, 11.3 Hz, 1 H, CH_2N) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 201.0, 137.8, 129.1, 128.6, 127.3, 58.5, 54.0 ppm. MS (ESI): *m*/*z* = 196 [M + H]$^+$. HRMS (ESI): calcd. for $C_6H_{14}NOS$ [MH]$^+$ 196.0249; found 196.0242.

General Procedure for the Preparation of Taurines: A solution of 30% H_2O_2 (5 mL) was dissolved in 98% formic acid (25 mL) at 0 °C and the mixture was stirred at 0 °C for 1 h to afford peroxyformic acid.[28] Thiazolidine-2-thione (5 mmol) was added portionwise to the peroxyformic acid solution at 0–5 °C in an ice bath. The resulting solution was stirred overnight and then warmed to room temperature. After filtering off any solid sulfur and removal of the solvents, the residue was crystallized from methanol, ethanol, or a mixture of methanol (or ethanol) and diethyl ether to afford colorless pure taurine or substituted taurines in good yields.

(*S*)-2-(Benzylamino)-3-phenylpropane-1-sulfonic Acid (4h): Colorless crystals; yield 1.30 g, 85%; m.p. 314–316 °C (decomp.). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 9.21 (br. s, 1 H, OH), 9.10 (br. s, 1 H, NH), 7.52–7.26 (m, 10 H, ArH), 4.47–4.38 (m, 1 H, CH_2N), 4.37–4.28 (m, 1 H, CH_2N), 3.66 (m, 1 H, CHN), 3.33 (dd, J = 3.8, 13.2 Hz, 1 H, CH_2S), 2.89 (dd, J = 11.0, 13.2 Hz, 1 H, CH_2S), 2.82 (dd, J = 9.8, 14.5 Hz, 1 H, CH_2Ar), 2.62 (dd, J = 2.4, 14.5 Hz, 1 H, CH_2Ar) ppm. ^{13}C NMR (100.6 MHz, [D$_6$]DMSO): δ = 136.6, 132.6, 130.0, 129.9, 129.5, 129.4, 129.2, 127.5, 57.1, 49.4, 48.1, 35.7 ppm. IR (KBr): $\tilde{\nu}$ = 3432 (br., OH, NH), 1256 (S=O), 1170 (S=O) cm^{-1}. HRMS (ESI): calcd. for $C_{16}H_{20}NO_3S$ [M + H]$^+$ 306.1158; found 306.1151.

1-Aminohexane-2-sulfonic Acid (4m): Colorless crystals; yield 798 mg, 88%; m.p. 335 °C (decomp.). ^{1}H NMR (300 MHz, D_2O, HDO as internal standard at δ = 4.67 ppm): δ = 3.25 (dd, J = 3.0, 13.8 Hz, 1 H, CH_2N), 3.15 (dd, J = 9.0, 13.8 Hz, 1 H, CH_2N), 2.95 (m, 1 H, CHS), 1.79 (m, 1 H, CH_2), 1.33 (m, 5 H, 2 CH_2 + 1 H of CH_2), 0.78 (t, J = 7.2 Hz, 3 H, CH_3) ppm. ^{13}C NMR (75.5 MHz, D_2O, HCO_2H as internal standard at δ = 166.3 ppm): δ = 57.47, 39.8, 28.6, 27.8, 22.4, 13.7 ppm. IR (KBr): $\tilde{\nu}$ = 3420 (br., OH, NH), 1221 (S=O), 1150 (S=O) cm^{-1}. MS (ESI): m/z = 181.7 [M + H]$^+$, 203.6 [M + Na]$^+$. HRMS (ESI): calcd. for $C_6H_6NO_3S$ [M + H]$^+$ 182.0845; found 182.0847.

Supporting Information (see also the footnote on the first page of this article): Experimental procedures for the preparation of thiazolidine-2-ones and L-cysteinolic acid, reaction of (*S*)-phenylaziridine and carbon disulfide and identification of the absolute configuration of the products, the analytical data and ^{1}H and ^{13}C NMR spectra of thiazolidone-2-ones, taurine, and substituted taurines.

Acknowledgments

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[1] For a review, see: J. X. Xu, *Chin. J. Org. Chem.* **2003**, *23*, 1–9.
[2] For a review, see: R. C. Gupta, T. Win, S. Bittner, *Curr. Med. Rev.* **2005**, *12*, 2021–2039.
[3] B. Wickberg, *Acta Chem. Scand.* **1957**, *11*, 506–511.
[4] For a review, see: R. J. Huxtable, *Physiol. Rev.* **1992**, *72*, 101–163.
[5] M. Satake, Y. Chiba, Y. Kohma, K. Yamamoto, M. Okabe, T. Mimura, T. Imanishi, C. Iwata, *Experientia* **1989**, *45*, 1110–1112.
[6] a) A. Obreza, S. Gobec, *Curr. Med. Rev.* **2004**, *11*, 3263–3278; b) S. M. Liebowitz, J. B. Lombardini, C. I. Allen, *Biochem. Pharmacol.* **1988**, *37*, 1303–1309; c) S. M. Liebowitz, J. B. Lombardini, P. S. Salva, *Biochem. Pharmacol.* **1987**, *36*, 2109–2114.
[7] a) W. J. Moree, G. A. van der Marel, R. M. J. Liskamp, *Tetrahedron Lett.* **1991**, *32*, 409–412; b) W. J. Moree, G. A. van der Marel, R. M. J. Liskamp, *J. Org. Chem.* **1995**, *60*, 5157–5169; c) D. W. P. Lowik, M. R. M. J. Liskamp, *Eur. J. Org. Chem.* **2000**, 1219–1228; d) C. Giordano, G. Lucente, A. Masi, M. P. Paradisi, A. Sansone, S. Spisani, *Bioorg. Med. Chem.* **2006**, *14*, 2642–2652; e) F. D. He, F. H. Meng, X. L. Song, W. X. Hu, J. X. Xu, *Org. Lett.* **2009**, *11*, 3922–3925.
[8] a) S. Gabriel, H. Ohle, *Ber. Dtsch. Chem. Ges.* **1917**, *50*, 804–808; b) P. Rumpf, *Bull. Soc. Chim. Fr.* **1938**, *5*, 871–888; c) J. W. Barnett, D. J. Dupre, B. J. Holloway, F. A. Robinson, *J. Chem. Soc.* **1944**, 94–96.
[9] a) H. Higashiura, H. Morino, H. Matsuura, Y. Toyomaki, K. Ienaga, *J. Chem. Soc. Perkin Trans. 1* **1989**, 1479–1481; b) D. Braghiroli, M. Di Bella, M. Saladini, *Tetrahedron: Asymmetry* **1996**, *7*, 831–836; c) D. Braghiroli, M. Di Bella, *Tetrahedron: Asymmetry* **1997**, *8*, 2209–2213.
[10] a) P. Rumpf, *Bull. Soc. Chim. Fr.* **1955**, 945–946; b) W. Zhang, B. Y. Wang, N. Chen, D.-M. Du, J. X. Xu, *Synthesis* **2008**, 197–200.
[11] a) R. L. Heath, H. A. Piggott, *J. Chem. Soc.* **1947**, 1481–1485; b) M. H. Gold, M. Skebelsky, G. Lang, *J. Org. Chem.* **1951**, *16*, 1500–1502.
[12] a) K. Higashiura, K. Ienaga, *J. Org. Chem.* **1992**, *57*, 764–766; b) W. J. Moree, G. A. Van der Marel, R. M. J. Liskamp, *Tetrahedron Lett.* **1992**, *33*, 6389–6392; c) M. C. F. Monnee, M. F. Marijne, A. J. Brouwer, R. M. J. Liskamp, *Tetrahedron Lett.* **2000**, *41*, 7991–7995; d) J. X. Xu, S. Xu, *Synthesis* **2004**, 276–282; e) B. Y. Wang, W. Zhang, L. L. Zhang, D.-M. Du, G. Liu, J. X. Xu, *Eur. J. Org. Chem.* **2008**, 350–355.
[13] F. M. Cordero, M. Cacciarini, F. Machetti, F. De Darlo, *Eur. J. Org. Chem.* **2002**, 1407–1411.
[14] a) J. X. Xu, *Tetrahedron: Asymmetry* **2002**, *13*, 1129–1134; b) N. Chen, M. Zhu, W. Zhang, D.-M. Du, J. X. Xu, *Amino Acids* **2009**, *37*, 309–313.
[15] L. B. Hu, H. Zhu, D.-M. Du, J. X. Xu, *J. Org. Chem.* **2007**, *72*, 4543–4546.
[16] a) J. X. Huang, F. Wang, D.-M. Du, J. X. Xu, *Synthesis* **2005**, 2122–2128; b) J. X. Huang, D.-M. Du, J. X. Xu, *Synthesis* **2006**, 315–319; c) H. Yu, S.-L. Cao, L. L. Zhang, G. Liu, J. X. Xu, *Synthesis* **2009**, 2205–2209.
[17] a) D. Enders, S. Wallert, *Synlett* **2002**, 304–306; b) D. Enders, S. Wallert, J. Runsink, *Synthesis* **2003**, 1856–1868.
[18] a) D. Enders, S. Wallert, *Tetrahedron Lett.* **2002**, *43*, 5109–5111; b) D. Enders, A. Moll, *Synthesis* **2005**, 1807–1816.
[19] D. Enders, D. Iffland, G. Raabe, *Synthesis* **2009**, 1682–1688.
[20] S. Ratner, H. T. Clarke, *J. Am. Chem. Soc.* **1937**, *59*, 200–206.
[21] a) M. G. Ettlinger, *J. Am. Chem. Soc.* **1950**, *72*, 4792–4796; b) H. J. Roth, H. Schlump, *Arch. Pharm.* **1963**, *296*, 213–217; c) Y. Nagao, Y. Hagiwara, T. Kumagai, M. Ochiai, T. Inoue, K. Hashimoto, E. Fujita, *J. Org. Chem.* **1986**, *51*, 2391–2393; d) R. A. Aitken, D. P. Armstrong, R. H. B. Galt, S. T. E. Mesher, *J. Chem. Soc. Perkin Trans. 1* **1997**, 2139–2146; e) M. M. Alhamadsheh, N. C. Waters, D. P. Huddler, M. Kreishman-Deitrick, G. Florova, K. A. Reynolds, *Bioorg. Med. Chem. Lett.* **2007**, *17*, 879–883; f) A. Osorio-Lozada, H. F. Olivo, *Org. Lett.* **2008**, *10*, 617–620.
[22] D. Delaunay, L. Toupet, M. Le Corre, *J. Org. Chem.* **1995**, *60*, 6604–6607.
[23] M. Fujita, Y. Miyashita, N. Amir, Y. Kawamoto, K. Kanamori, K. Okamoto, *Polyhedron* **2005**, *24*, 1991–2001.
[24] T. A. Foglia, L. M. Gregory, G. Maerker, S. F. Osman, *J. Org. Chem.* **1971**, *36*, 1068–1072.
[25] The specific rotation of (*R*)-5-phenylthiazolidine-2-thione (**2f′**) is unknown. To determine its configuration and optical purity, it was further oxidized into the known (*R*)-1-phenyltaurine (**4f′**) and compared with the reported data. See the Supporting Information and also J. X. Xu, N. Chen, *Faming Zhuanli Shenqing Gongkai Shuomingshu* **2009**, CN101337914 [*Chem. Abstr.* **2009**, *150*, 167868].
[26] a) H. Wenker, *J. Am. Chem. Soc.* **1935**, *57*, 2328; b) M. Zhu, L. B. Hu, N. Chen, D.-M. Du, J. X. Xu, *Lett. Org. Chem.* **2008**, *5*, 212–217.
[27] J. Wu, Z. B. Luo, L. X. Dai, X. L. Hou, *J. Org. Chem.* **2008**, *73*, 9137–9139.
[28] **CAUTION!** Performic acid is potentially explosive. Although no explosion occurred during our experiments, attention should be paid towards safety.
[29] K. Schank, F. Werner, *Liebigs Ann. Chem.* **1979**, 1977–1991.
[30] D. H. R. Barton, D. P. Manly, D. A. Widdowson, *J. Chem. Soc. Perkin Trans. 1* **1975**, 1568–1574.

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